THESIS

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

SESSION 2020-2023

A COMPARATIVE STUDY OF MEPHENTERMINE AND PHENYLEPHRINE IN THE TREATMENT OF HYPOTENSION DURING SPINAL ANAESTHESIA FOR CAESAREAN SECTION

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SANTOSH DEEMED TO BE UNIVERSITY

NO. 1, SANTOSH NAGAR,

GHAZIABAD-201009, NCR DELHI, INDIA

DEPARTMENT OF ANAESTHESIOLOGY

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Department of Anaesthesia
Santosh Medical College & Hospital
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CERTIFICATE BY THE HEAD OF THE DEPARTMENT

This is to certify that the thesis titled **"A comparative study of mephentermine and phenylephrine in the treatment of hypotension during spinal anaesthesia for caesarean section"** is a bonafide research work carried out by **Dr. Jahnavi Tomar** in partial fulfilment of the requirements for award of the degree of M.D. anaesthesiology will be based on bonafide work carried out by her .

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INTRODUCTION

Spinal anaesthesia is one of the most common regional block techniques used in clinical practice. the first subarachnoid block was given by August Bier in the year 1885, after that Adriani and his associates in the year 1940's developed a well-established and standardized safe technique of analgesia and became popular anaesthesia in the field of obstetrics (1)

Anaesthesia to woman in labour, specifically those who are admitted for caesarean section, requires a high degree of anaesthesiologists' care to take care of two lives, the mother and the foetus. One of the efficient ways to reduce the labour pain is "Neuraxial anaesthesia".

Nowadays, worldwide caesarean section is one of the common surgical procedures and spinal anaesthesia is the most used technique (2); (3) It is reported that spinal anaesthesia provides a better and low-cost anaesthesia technique for any elective caesarean sections compared to epidural anaesthesia (4) However, risk of post spinal anaesthesia complication in women undergoing elective caesarean section is also reported to be as many as 85% (4)

Several studies in the recent past have also reported that the increased risk for complications such as hypotension after spinal anaesthesia, and persistent hypotension might lead to other complications including hypoperfusion of the placenta that can cause foetal distress, acidosis and low (<7) Apgar score (5) (6) (7) Impaired cardiovascular function in pregnant females experiences sympathetic block due to those who receives the spinal anaesthesia and thereby decreases venous return to the heart and resulted in hypotension.

In general, spinal anaesthesia for cesarean delivery caused hypotension could have various detrimental effects to both the mother and neonate. These harmful consequences of hypotension include reduced blood flow to the uterus and the placenta, which leads to hypoxic damage to the fetus may lead acid base imbalance, and poor APGAR.

Studies earlier have claimed that the possible treatment options for hypotension might be suitable and convenient position to avoid unwanted aortocaval compression of the

patient with displacement of pregnant uterus, increasing available vascular volume by using crystalloids and colloid liquids, raise the heart rate with the use of ephedrine, cardiac output and peripheral vascular resistance, increasing the peripheral vascular resistance and mechanical compression of the lower limbs before or after the spinal anaesthesia is placed with the use of α1-agonists (8)(9)(10)(11) However, vasopressors being used traditionally to prevent and manage hypotension after neuraxial anaesthesia could lead to an increase systemic vascular resistance and rise in the mean arterial pressures(12)

Even then, the use of vasopressors to counteract the hypotension after neuraxial anaesthesia in obstetrics is still being a puzzle. Therefore, identification of suitable agent(s) to prevent and manage hypotension during spinal anaesthesia for any surgical procedures including caesarean sections has been the subject of much detailed investigations and controversies (13)

Several studies have reported that the use of intravenous vasopressors has been the main stay in treating hypotension caused by spinal anaesthesia (14)(15)(16). Such vasopressors so far in practice includes ephedrine, methoxamine, metaraminol, mephentermine, phenylephrine, and epinephrine. Mephentermine, one of the sympathomimetic drugs acting both directly and indirectly with both alpha and beta adrenergic agonistic action. With the use of mephentermine, increase in both the systolic and diastolic blood pressure with augmentation on the cardiac output and increased the peripheral vascular resistance (5) However, based on our search and other literature (17); (18) only limited studies have been conducted and reported about the use of mephentermine in pregnant women and compared the effects on managing the spinal anaesthesia induced hypotension in obstetric patients.

Phenylephrine, a selective α1-adrenergic receptor agonist, is another drug that is commonly used for the treatment of hypotension (19)(20);. It has been reported that the use of phenylephrine causes a rapid onset of action and is also commonly used in treating hypotension due to spinal anaesthesia in pregnant females. It is also reported that the use of phenylephrine could increases the systolic blood pressure by peripheral vasoconstriction and causes baroreceptor-mediated reflex bradycardia and decreased cardia output (21), however, no adverse effects on the foetus in patients undergoing elective operations has been reported (5); (22)

However, there is paucity in studies comparing the efficacy of mephentermine and phenylephrine in controlling the hypotension caused by spinal anaesthesia during caesarean sections in western part of the Uttar Pradesh, India.

Therefore, the present study has been designed to study the efficacy of mephentermine and phenylephrine and compare the effects of these two drugs in regulating the blood pressure, heart rate, and incidence of nausea, vomiting and any other possible effects of the drugs in a tertiary care hospital at Ghaziabad, UP.

SAMPLE SIZE CALCULATION

Sample Size: The required sample size was calculated with reference to a published A "Comparative Study on The Role of Phenylephrine and Mephentermine in the Treatment of Hypotension During Spinal Anaesthesia for Caesarean Section" by Tridib Choudhury et al(23) and using the formula given below:

$$n= 2*[z_{\alpha}+z_{1-\beta}]^2*SD^2/d^2$$

Z_{α} =1.96 at 5% level of significance

SD= standard deviation

d= effect size

$Z_{1-\beta}$=1.28 at 90% power

D=1.24812, d=1.2111

After putting the values in the above-mentioned formula,

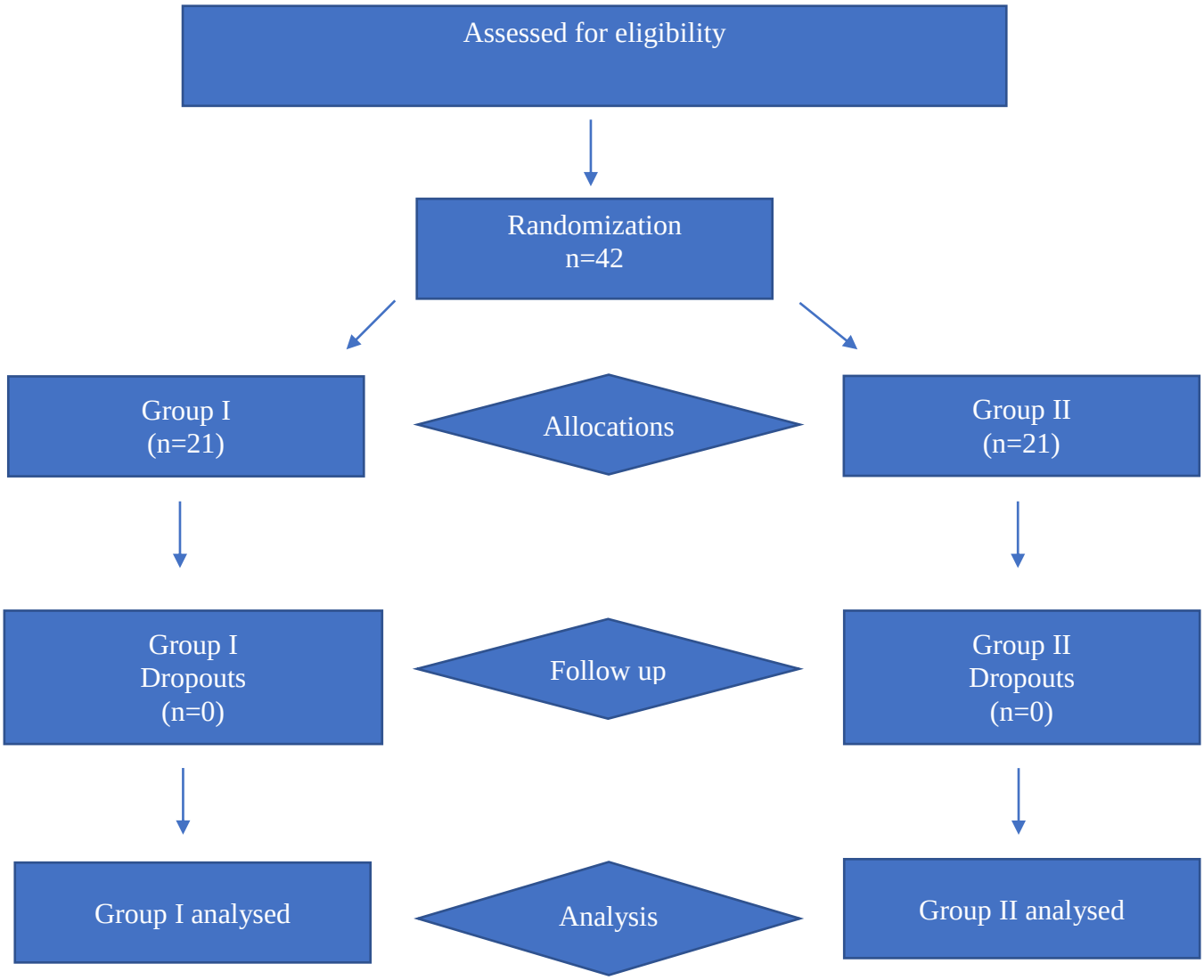
n=20.9 ≈ 21 in each group.

Group I- Patients receiving IV bolus of phenylephrine 100 mcg

Group II- Patient receiving IV bolus of mephentermine 6 mg

Total sample size = 42.

Consort flow chart



AIM & OBJECTIVES

Aim:

- To compare the effects of bolus IV phenylephrine and mephentermine in maintaining arterial blood pressure in women undergoing caesarean section.

Objectives:

Primary objective:

- Studying the effects of phenylephrine and mephentermine in maintaining arterial blood pressure.

Secondary objective:

- To evaluate and compare the effect of these two drugs on the heart rate.
- To evaluate and compare the time taken for recovery from hypotension using these drugs.
- Comparison of the incidence of nausea, vomiting and other effects of these two drugs.

REVIEW OF LITERATURE

Spinal anaesthesia, a form of blocking the central neuraxial system is one of the commonly used techniques for caesarean section globally. Injection of local anaesthetic by itself or along with adjuvant solution into the sub-arachnoid space would temporarily interrupt the nerve transmission. Therefore, it is considered to be one of the regularly followed methods for regional anaesthesia including caesarean section. One of the most notable advantages of using this method of anaesthesia is that the mother stay awake for the birth that could possibly initiate the early bonding with the baby and further avoiding the risks of general anaesthesia that could cause postoperative complications including pain. Despite the general anaesthesia, use of spinal anaesthesia in obstetrics patients could secure specific considerations that might be because of maternal anatomy and physiology that have implication on clinical aspects and could lead to harmfulness to the mother and the foetus during anaesthesia.

Therefore, understanding the maternal physiological changes that would happen during pregnancy is the basic fundamental to obstetric anaesthesia with reference to the spinal anaesthesia. The most crucial factors are thought to be knowing about the perioperative effects of spinal anaesthesia on the foetus, the relationship between spinal anaesthesia and hypotension, and the pharmacology of the drugs used to treat hypotension.

Physiological Changes in Pregnancy:

Practically, every system of the mother is being affected by pregnancy, primarily the cardiovascular system. Several evidence are available to support the anatomical and physiological changes (24) (25)

Body Weight and Composition:

The average pregnancy weight gain is 17% of the pre-pregnancy weight (12 kg roughly),

The uterus adds on 1 kg, amniotic fluid 1 kg, foetus and placenta 4 kg and body fluids increases 2 kg each blood and interstitial fluid, and deposition of fat 4kg.

1st trimester the wait gain is 1-2kg, 2nd 5-6 kg and 3rd 5-6 kilograms.

Blood Volu7me Changes:

The expansion of plasma volume is the primary cause of the blood volume rise from 60–65 to 80–85ml kg-1. When the baby is 30-32 weeks old, the plasma volume increases to its highest level. The rise in red cell volume is less than that of plasma volume. As a result, the haematocrit decreases, and the haemoglobin concentration drops from 14 to 12 g dl-1.

Changes in the Cardiovascular System:

Within the first 10 to 12 weeks, there is a 1.5 litre min-1 rise in cardiac output to go along with the increase in blood volume. By the late pregnancy, heart rate and stroke volume both increase by around 17%, which results in an approximately 44% increase in cardiac output. This is needed to keep up with the increasing oxygen usage. During pregnancy, the systemic vascular resistance decreases.

Changes in the Blood Pressure:

Pregnancy does not result in a substantial change in systolic blood pressure, but until 28 weeks of gestation, there may be a considerable reduction in diastolic blood pressure below the pre-pregnancy range (26)**.** But during pregnancy, the mean arterial pressure essentially stays the same. Despite an increase in maternal cardiac output, there is no discernible rise in central vein and pulmonary capillary wedge pressure during pregnancy. (27)

The gravid uterus has an impact on the mother's circulation due to its weight and size as well as the blood it holds. By pushing on the inferior vena cava, the gravid uterus limits venous return, which decreases from an average normal level of 11.4 cm H20 to roughly 24 cm H20 (28). When the patient is supine and the pressure of the uterus and foetus resting on the inferior vena cava is greatest. Due to this, supine hypotension syndrome develops. (29) The hypotension results in various side effects leading to dizziness, nausea, and vomiting. It also affects the foetal circulation. The resultant hypotension may adversely affect the foetus by compromising placental blood flow. Parturient may be symptom free or may complain of distressing symptoms of fainting

or nausea and vomiting. In up to 90% of patients, moving the uterus to the left or raising the right hip returns the blood pressure to normal. (29). Therefore, a wedge under the right hip is used routinely in caesarean section to displace the uterus to left. Epidural vein puncture is more prone to happen when the epidural vasculature is engorged. During spinal anaesthesia, less local anaesthetic drugs are needed because of engorged arteries(30)

Metabolism and Respiration:

Oxygen requirement: 30 to 40% more oxygen consumption due to increased metabolic demand of the body.

Lung Volumes and Capacity:

Another crucial area of the parturient's anatomy is the mechanics of breathing; the expanding uterus shifts the diaphragm cephalad, reducing the functional residual capacity, but leaving the vital capacity and the inspiratory capacity unaffected due to an increase in Antero posterior thoracic diameter. Despite an increase in alveolar ventilation of 70% due to an increase in tidal volume by 40% and respiratory rate by 15%, fast desaturation happens during apnoea because to decreased functional residual capacity and higher oxygen demand.

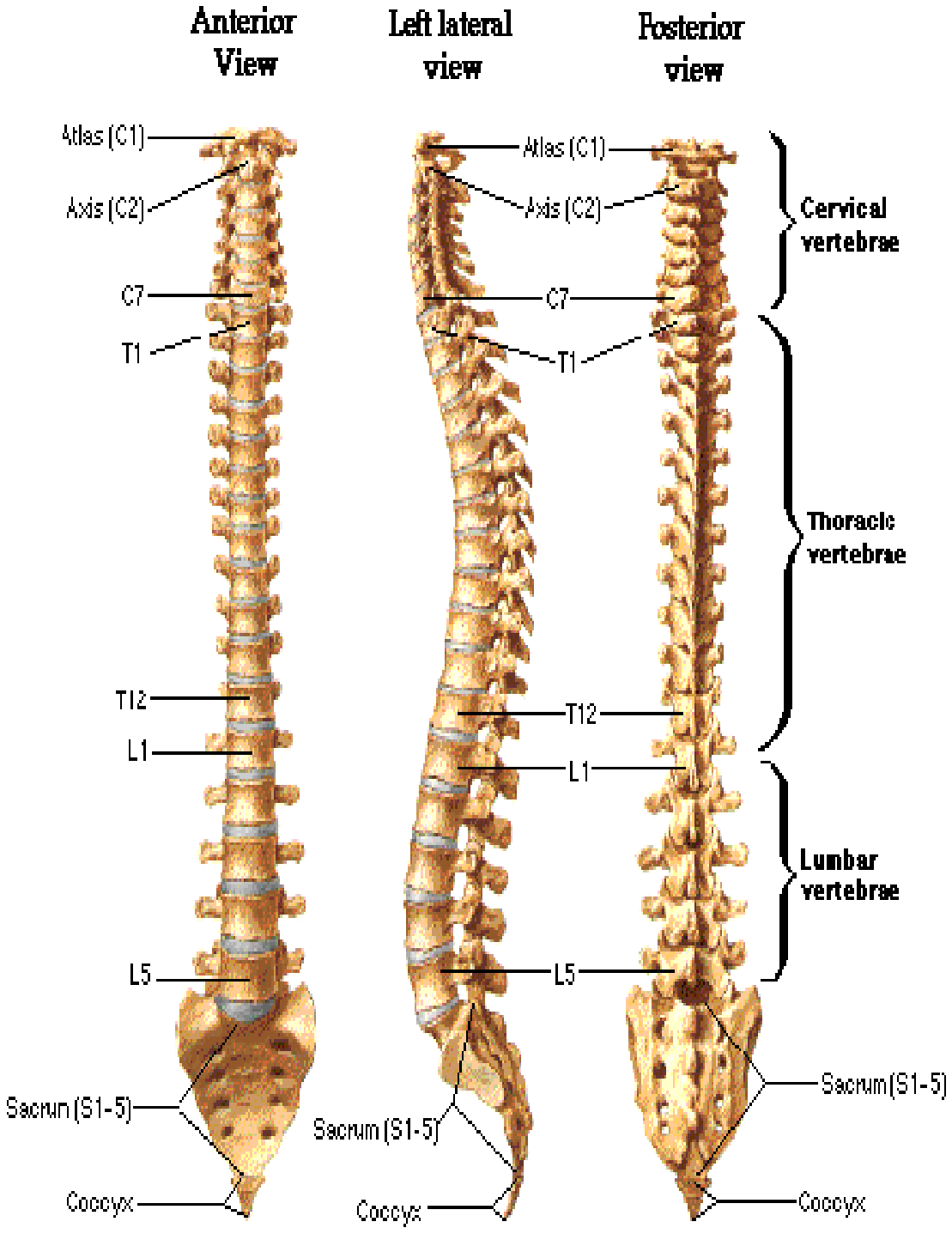
Ventilation:

During pregnancy, minute ventilation rises by 45%, beginning to rise early in the first trimester. The tidal volume alters as a result. Although it marginally decreases during second trimester, respiratory rate is mostly unaffected by pregnancy. Oestrogen also contributes to increased ventilation. Additionally, oestrogen aids in enhanced ventilation.

Anatomy of the Human Vertebral Canal and the Spinal Cord

Vertebral Canal: The extension from the foramen magnum to the sacral hiatus called as the "Vertebral Canal," normally contains seven cervical, twelve thoracic, five lumbar and five sacral, formed by the dorsal spine, pedicles ad lamina of the successive vertebrae. The network of interlocking ligaments that holds the vertebrae together consists of the intervertebral discs, anterior longitudinal ligament and

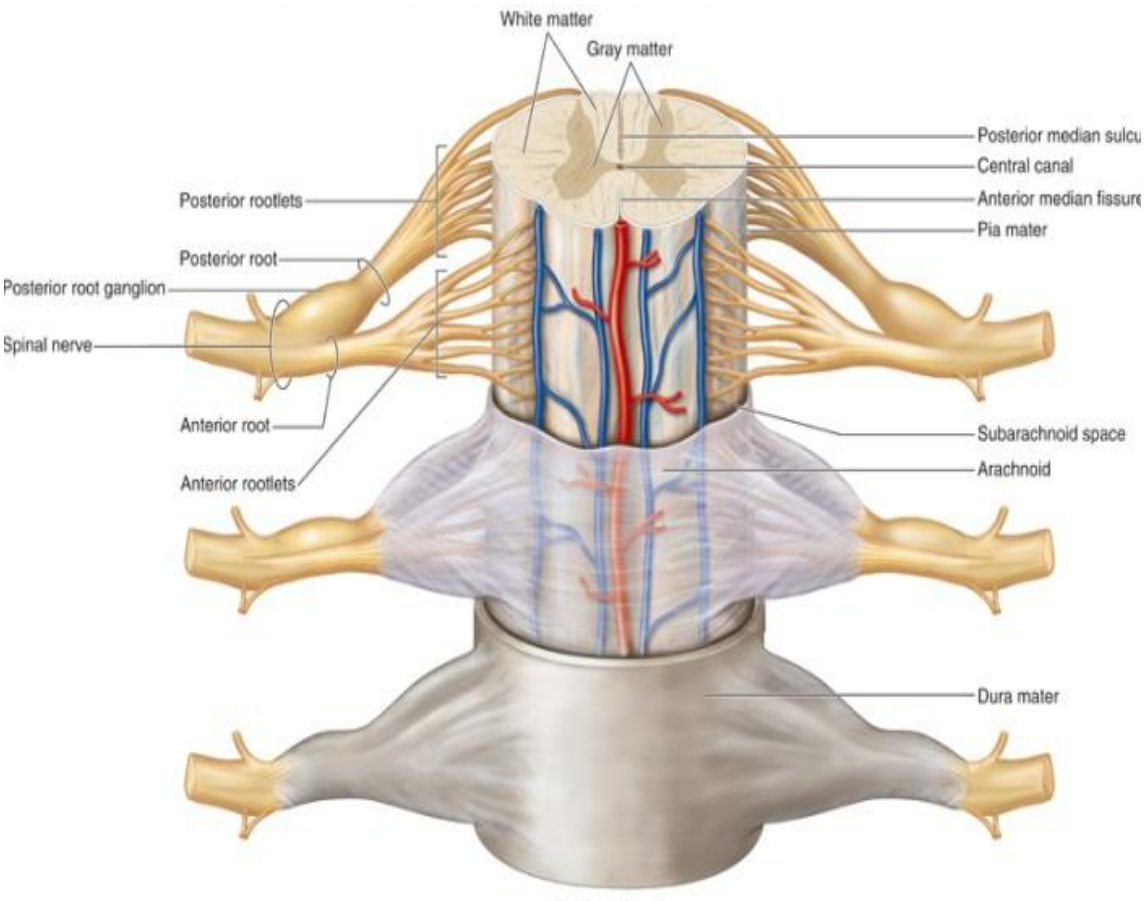
posterior longitudinal ligaments, ligamentum flavum, interspinous ligaments, and supraspinous ligaments.



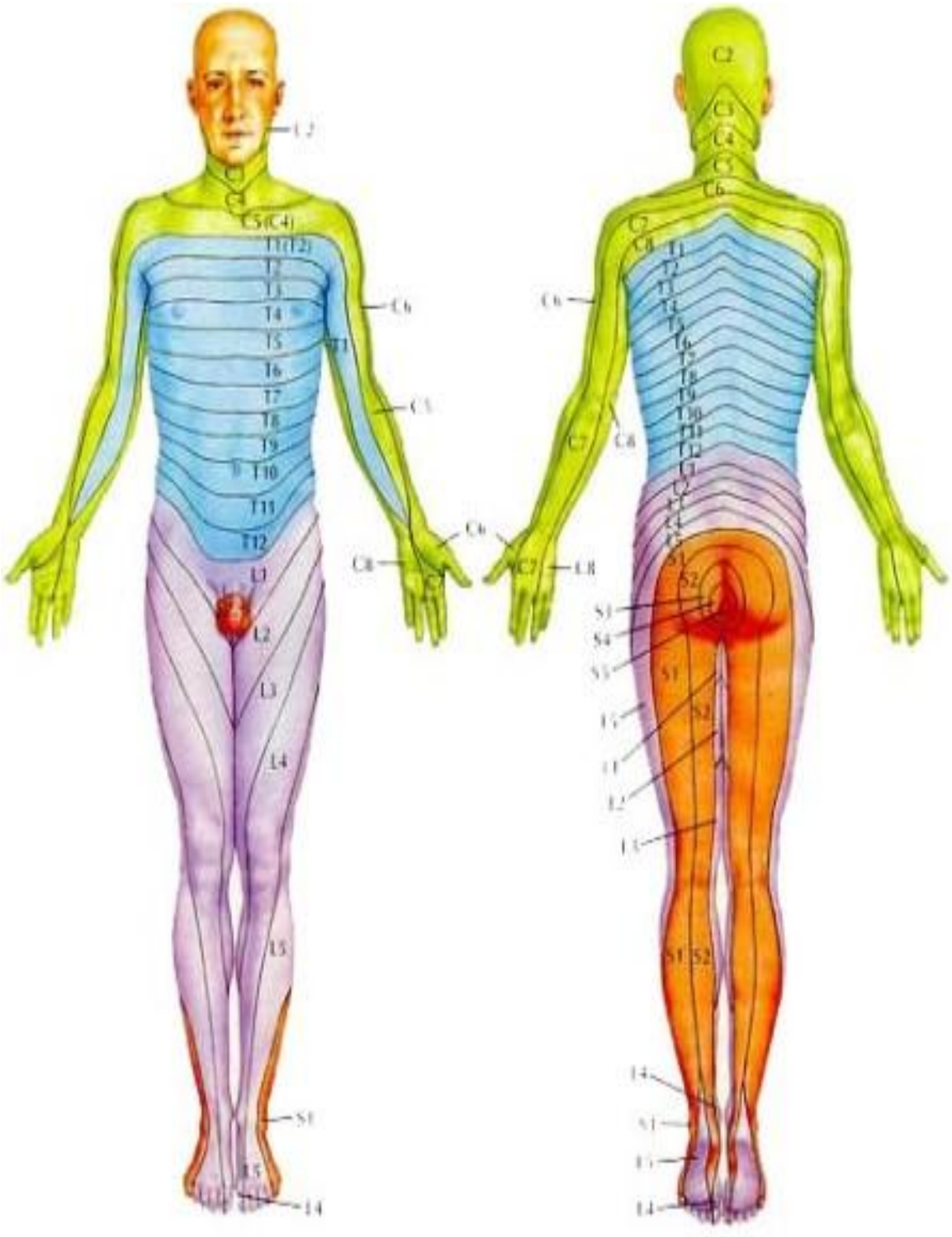
Spinal Cord: The spinal cord runs in the vertebral column. Medulla oblongata continues as the spinal cord, which starts at upper border of the atlas and ends at in the conus medullaris. In adults the spinal cord ends at L1 and in the infants it ends at the lower border of L3. The spinal cord is surrounded by 3 membranes i.e., piamater,

arachnoid mater and the duramater. Piamater is the innermost then comes the arachnoid mater followed by the duramater outside.

Pia mater closely adherent to the spinal cord, it is a very vascular. Arachnoid mater is membrane of vessels tightly adherent to the duramater. The space in between the arachanoid mater and the paimater is filled with the cerebrospinal fluid, blood vessels for the supply to spinal cord and denticulate ligaments. The longitudinally organized fibro elastic membrane called as the dura mater is the outermost membrane of the spinal cord and is directly extended from duramater present at the cranium to duramater of the spine (starting from the foramen magnum to S2). Outside the duramater there is epidural space extending from the foramen magnum to the sactum. The ligamentum flavum and interspinous ligament run justjust posterior to the epidural space. The spinal cord ends at L1 in adults to avoid any damage to the spinal cord the routine lumber puncture is done in spaces below L2, routinely used spaces are L3-L4, L4- L5, and L5- S1 in adults.



Dermatomal Chart



CEREBROSPINAL FLUID:

The cerebrospinal fluid (CSF) is a clear fluid found in the subarachnoid space of the brain and spinal cord, and it is also found in the ventricles of the brain. It is an ultra-filtrate of plasma. It is produced in the choroidal plexus ependymal cells present in the ventricles, secreted at a rate of 0.3-0.4 ml/minute. Volume in adults- 120-150 ml.

In the sub arachnoid block the spread of local anaesthetic is mediated by the CSF, the specific gravity and baricity of the drug and CSF plays the major role on the neuraxial blockadge the specific gravity of CSF is 1.007 and baricity is 1.000.

SPINAL ANAESTHESIA

Mechanism:

On injecting the solution of local anaesthetic agent into the sub arachnoid space at the level below L2 vertebra. Both the spinal cord and the peripheral nerve roots can be reached through the area where cerebrospinal fluid is flowing. Because they are not protected by epithelium in the cerebrospinal fluid, local anaesthetic is accessible to the nerve roots that leave the spinal canal. Thus, during the spinal anaesthesia ventral nerve roots are blocked, preventing afferent impulses from escaping through them. The Na^+ gated channels block the electrical impulse. (31)

Order of block :

Sympathetic : Unmyelinated sympathetic fibres are blocked first.

- Sensory: Sensory block comes after the sympathetic block
- Motor: In the last motor block is achieved, and 2 segments above the blockade of sensory block.
- Temperature – Cold sensation is blocked before warm.
- Pinprick sensation carrying fibres
- Touch conveying fibres
- Deep pressure sensation carrying fibres

- Somatic motor sensation carrying fibres.
- Vibration sense and proprioception conveying fibres

Local Anaesthetics Spread:

Cerebrospinal fluid dilutes the locally administered anaesthetic solution. The baricity of the injected fluid determines spread as well. The density of CSF at a specific temperature to that of a local anaesthetic solution at the same temperature, this ratio is known as baricity.. Hypobaric – < 1.0000 , specific gravity < 1.0069 , Hyperbaric - > 1.0000 or specific gravity > 1.0069. Dextrose is added to isobaric solution to produce hyperbaric solution. And distilled water is added to the isobaric solution to prepare a hypobaric solution.

In the CSF, under the influence of gravity Isobaric solutions do not move. Since hyperbaric solutions are heavier than CSF, they settle in the subarachnoid space's most dependent region, which is influenced by the patient's position. Hyperbaric solutions migrate toward the thoracic kyphosis in supine patients. The nerves innervating the surgical site are reached by a hypobaric solution that floats up. The amount of drug injected and the baricity of the drug determines the degree of the block. The concentration of local anaesthetic solution rapidly decreases after injection into the subarachnoid region. Due to mixing with CSF and subsequent absorption into the spinal cord and nerve roots, the first rapid fall is produced. Local anaesthetic solution is mostly absorbed by spinal and epidural vessels. There is no hydrolysis or degradation occurring in the CSF. The medicine is either metabolised in the liver or in plasma by pseudo cholinesterase, depending on the type of medication administered. The rate of absorption and addition of the adjuvant determines the length of the blockage. By vasoconstriction we can lengthen the anaesthesia as the rate of absorption will be decreased.

Effects of Subarachnoid Block's Circulation:

Post spinal hypotension

Subarachnoid block's in obstetric patients most frequent adverse effect is hypotension. Several therapies, including pelvic tilts, pelvic wedge, prophylactic fluid

administration, and the use of vasopressors, have been in use from the past several years to lower the incidence of maternal hypotension. Effect of neuraxial block on the cardiovascular system(32)

- Vasodilatation of vessels.
- Loss of chronotropic and inotropic drive, together with a decrease in cardiac output, are caused by the blockage of cardiac efferent sympathetic fibres from T1 to T4.
- Bainbridge reflex causing bradycardia.
- Marey's law causing tachycardia.
- After systemic absorption of local anaesthetic agent, there is a decrease in cardiac output along with relaxation of vascular smooth muscle and beta-adrenergic blockade.
- Adrenaline, when administered as an adjuvant, stimulates the body after absorption by decreasing the systemic vascular resistance and increasing the cardiac output. The total result is expected to be a lower mean arterial pressure than would have occurred without the administration of adrenaline.

Effect of subarachnoid block on foetus:

Subarachnoid block may have a direct impact on the foetus due to the effects of local anaesthetics or vasopressors. indirectly by the physiological modifications brought on by the mother's sympathetic inhibition, which results in hypotension. There is no autoregulatory system in the uterine vessels. There is no autoregulatory system in the uterine vasculature. As a result, perfusion pressure and uteroplacental blood flow are directly correlated.(26)

Hypotension during caesarean section reduces the placental blood flow which directly impacts the foetus as the saturation of the foetal blood is low. If the hypotension is not managed promptly during a caesarean section the foetal outcome becomes poor. Some studies have also reported that if the maternal blood pressure is less than

100mmhg(SBP), It causes foetal bradycardia. [33],[34] and acid base imbalance and some studies also have suggested that prolonged low SBP may lead to neurobehavioral abnormalities.[35] The drug administer in spinal anaesthesia in a low concentration has shown no adverse effect on the foetus. Low concentration of drug in the plasma doesn't cause any foetal side effect. As uterine arteries only have alpha receptors and react to sympathomimetic agents, a vasopressor without uterine vasoconstriction characteristic is ideal for use in obstetrics. A vasopressor with alpha agonist properties might potentially have a vasoconstrictive impact on the uteroplacental vasculature, which would aggravate the state of the foetus.

PHARMACALOGY :

Mephentermine:

It is a manmade sympathomimetic drug; it is structurally similar to methyl amphetamine.

Pharmacodynamics:

By releasing noradrenalin from its storage sites, mephentermine indirectly stimulates beta adrenergic receptors(predominantly) and alpha-adrenergic receptors are stimulated less of the sympathetic system. Cardiovascular stimulation is the predominant effect of therapeutic dosages of mephentermine. The myocardium experiences a positive inotropic response. In most patients, the force of contraction and cardiac output rise, and in certain cases, the stroke volume does too.

It improves ventricular conduction velocity by reducing atrioventricular conduction velocity and the AV node's refractory period. The drug has a chronotropic impact on the sa node, although this effect is usually negated by an increase in vagal activity brought on by high BP and increases the heart rate.

Mephentermine directly dilates the skeletal and mesenteric vascular beds' arteries and arterioles. The heart receives a greater venous return. Furthermore, increases cardiac output, which increases both systolic and diastolic blood pressure.

Pharmacokinetics:

The onset of action- immediately if given IV and takes up to 5-15 minutes if given IM.

Excretion- It is quickly broken down by the liver's demethylation and hydroxylation .

Indication: post spinal hypotension, hypotension caused due to anaesthesia, nerve block, shock.

Side effects:

- Tachycardia
- Anxiety
- Insomnia
- Hypertension
- Arrythmias

Dose:

- IM: 30-45mg, 10-20 min before the subarachnoid block for prophylaxis.
- Hypotension secondary to spinal anaesthesia (Treatment)
  IV: 10-25 mg iv bolus. The bolus can be repeated to maintain the blood pressure.
  IV infusion: A solution of 1mg/ml concentration can be started as infusion and the dose can be alerted as per the requirement.

Phenylephrine:

Phenylephrine is a man-made directly acting sympathomimetic drug. It is chemically related to epinephrine and ephedrine.

Pharmacodynamics:

A potent post-synaptic alpha-1 receptor stimulant, phenylephrine has little impact on the heart's beta receptors. It is directly acting sympathomimetic drug. Following injection, it causes noticeable peripheral vasoconstriction, which raises both systolic and diastolic blood pressure. It causes slight decrease in the cardiac output while increases the peripheral vascular resistance significantly. Its actions on the alpha receptors, causes mydriasis and vasoconstriction in the skin, mucous membranes, and mucosa.

Pharmacokinetics:

Onset of action-

- IV- immediately, the duration of action is 15-20 minutes.
- IM- 10-15 minutes, the duration of action 0.5 to 2 hrs (IM) 50 to 60 mins (SC)
- Topical- 15-20 minutes, the duration of action 30 to 40 mins.

Indications:

- Hypotension without bradycardia
- Bradycardia
- Septic shock
- Cardiogenic shock
- Neurogenic shock
- Haemorrhagic shock

Side Effects:

- Tissue necrosis by extravasation
- Cardiovascular system: Arrhythmias and reflex bradycardia,
- Central nervous system: Restlessness, excitability, and headache.

Dosage and Administration:

Mild to moderate hypotension:

- Subcutaneous and intramuscular: 2 – 5 mg.
- Intravenous: 0.2mg, range from 0.1 – 0.5mg.
- Severe hypotension:

IV infusion: 100-180 mcg/min initial dose and 40-60mcg/min for maintenance.

Post spinal hypotension:

- Subcutaneous or Intramuscular: 2 –3 mg, 5 minutes before the spinal anaesthesia
- Intravenous bolus: 100-200 mcg.

Studies on treatment of post spinal hypotension in caesarean section:

Dinesh Sahu et al(36) in the year 2003 conducted a study to determine ephedrine, mephentermine and phenylephrine in bolus form for maintenance of hypotension post subarachnoid block during caesarean section. The study was conducted by enrolling 60 patients grouped into three namely, Group P: received 100µg of Phenylephrine; Group E: received 6 mg of Ephedrine; and Group M: received 6 mg of inj. Mephentermine. This study concluded that all the three vasopressors are effective in maintenance of blood pressure. Inj. ephedrine and inj. mephentermine causes tachycardia and relative bradycardia with the inj. phenylephrine. And it also has a quick action.

A comparative study was conducted by **Moran DH et al**(37) in the year 1991 using Ephedrine and Phenylephrine to prevent maternal hypotension following spinal anaesthesia for caesarean section. Finally, they came to the conclusion that phenylephrine's efficacy is similar to that of ephedrine in the treatment of hypotension in c- section after subarachnoid block. They also mentioned that it has almost no side effects on the foetal outcome if the drug is given in small amount to parturient.

In a systemic review conducted by **Anna Lee et al** (2002)(38) to compare Ephedrine with Phenylephrine for the preventing and treating the post spinal hypotension during caesarean section. In this study phenylephrine came out a preferred choice over ephedrine, as it had better outcomes of maternal hypotension and foetal acid base status.

In 1996, **Thomas D G et al**(15) conducted a randomized control trial to compare the phenylephrine and ephedrine's efficacy when used for treating the hypotension in case of post spinal hypotension in LSCS. For the purpose of maintaining maternal arterial pressure, boluses of either phenylephrine 100 g or ephedrine 5 mg were given to 38 females undergoing elective c-section under spinal anaesthesia. Every minute blood pressure and heart rate were recorded, they also noted the effect of respective drugs on the APGAR of the neonate. In their result they found out phenylephrine a better choice of drug for post spinal hypotension during c- section.

Ngan Kee and co-workers in the year 2004(39) did a comparative study for three different BP thresholds for phenylephrine infusion regimens. The umbilical artery pH was the primary outcome metric that they compared**.** They prepared infusion dose of phenylephrine 100 mcg/ml and started at 100 mcg/min after spinal anaesthesia was given and continued till they achieved the desired assigned baseline value of systolic blood pressure. They concluded that phenylephrine should be titrated according to the baseline values of SBP in a case of post spinal hypotension in caesarean section.

A M Cyna et al., in 2006(40) conducted a randomized controlled trial study to compare the therapies to prevent hypotension multiple vasopressors with the placebo therapy to treat hypotension in caesarean section under spinal anaesthesia. 75 trials were performed on 4624 parturients. They discovered that crystalloids were better than no preloading with fluids, ephedrine was found out be better than crystalloids in treating hypotension. Between phenylephrine and ephedrine, no drug is superior in terms of treating hypotension. It was also found out that ephedrine in higher doses causes tachycardia and hypertension. Final interpretation was made that all of the above are used to treat hypotension but none of them eliminates the hypotension after spinal anaesthesia in a case of lower segment caesarean section.

S. Ram Nathan et al (1988)(41) performed a study to treat hypotension because of epidural anaesthesia by vasopressor therapy. They took 127 females undergoing elective LSCS, they observed changes in maternal homodynamic and acid-base balance of neonate. They made three groups. In group one females requiring no vasopressor, group two females SBP <90 mmHg and MAP< 67mmHg inj. Ephedrine 5mg was given and group three if SBP <83mmg and MAP <62 mmHg inj. Phenylephrine 100 mcg was given. Transient hypotension does not influence the acid-base state of the newborn, The cardiac preload is raised by phenylephrine and ephedrine. When used to treat maternal hypotension, phenylephrine, an alpha agonist, does not result in foetal acidosis.

David Cooper et al (2002)(42) did a study to compare the effects of inj. phenylephrine 100mcg, inj. ephedrine 3mg/ml & inj. phenylephrine 50 mcg/ml & inj. ephedrine 1.5mg/ml in infusion for maintaining the baseline blood pressure during spinal anaesthesia for LSCS. They discovered that compared to the ephedrine group, the phenylephrine group and the combination group experienced less foetal acidosis.

The SBP was similar is all the groups. The Ephedrine group had more tachycardia as compared to other groups. Less nausea and vomiting in phenylephrine group. In the end they concluded that there is no advantage of combination group as there was more nausea and vomiting in combination group. They came to the conclusion that there were no appreciable variations in the foetal acid-base status or lactate concentrations, despite the fact that ephedrine had more favourable effects on uterine and placental circulations than phenylephrine.

Kansal et al(17) **in 2005** conducted a randomized comparative study on IV infusion of mephentermine and ephedrine for the maintenance of maternal systolic blood pressure post spinal anaesthesia during a lower segment caesarean section. Intravenous Infusions of mephentermine and ephedrine were given to the females who developed hypotension post spinal anaesthesia, 30 each group. Haemodynamic parameters, requirement of vasopressors and time of recovery from the hypotension were similar in both the groups. Acid-base balance and APGAR score of the new-borns were similar. They ultimately came to the conclusion that Mephentermine can be administered as safely and successfully as Ephedrine to treat hypotension in females undergoing spinal anaesthesia for caesarean section.

Lauckner W et al in 1978(43) conducted a study on ten late-pregnant women with hypotension were evaluated using the quantitative sphygmometry technique, prior to and following the intravenous administration of 30 mg of mephentermine. The direct electronic timing of the pulse wave velocity and the bloodless graphic recording of blood pressure. Significantly elevated blood pressure results, because of increased store volume. While in his findings heart rate and peripheral vascular resistance was unchanged. He came to a conclusion that this kind of response is good for foetal blood flow, and hence in his study he found out that mephentermine is appropriate drug for treatment of hypotension during pregnancy.

Ngan Kee et al (2003)(44) has studied the variables influencing the umbilical artery standard base excess and pH in 337 elective C- sections carried out under spinal anaesthesia. They finally came to a result that, Ephedrine shouldn't be administered before to delivery to reduce the danger of foetal acidosis, alpha-agonists such phenylephrine or metaraminol should be administered to lessen the severity of hypotension within the shortest possible time between the uterine incision and birth.

Mercier FJ et al (2007)(45) observed the data on hypotension during spinal anaesthesia for caesarean sections at the Medline database, it was discovered that, if not treated, it occurs often (55 to 90% of the time). Colloid preload is preferable as a second line of defence. Although it has a limited preventive effect, ephedrine has long been the preferred vasopressor and it can also cause foetal acidosis and cardiovascular side effects. In this study they also found out that phenylephrine given prophylactically with or without ephedrine is equivalent to ephedrine and with lesser maternal and foetal side effects and finally they came to conclusion that post spinal hypotension during caesarean section should be treated promptly without a delay with vasopressors like phenylephrine and ephedrine and co-loading should also be done.

Ayorinde et al (2001)(46) conducted and double blind randomised controlled trial to evaluate prophylactic IM phenylephrine and ephedrine in 108 patients undergoing elective C-section under spinal anaesthesia. Four groups were made. 1st Group inj. phenylephrine 4 mg i.m., 2nd group received inj. phenylephrine 2 mg i.m., 3rd group received inj. ephedrine 45 mg i.m., 4th was the control group received. injection of saline i.m., Immediately after the spinal anaesthesia. They came to the conclusion that prophylactic intramuscular administration of inj. phenylephrine and inj. ephedrine decreases the severity hypotension and reduces the amount of bolus needed for hypotension post spinal anaesthesia for Caesarean delivery.

Afshari A et al (2006)(47) reported that foetal acidity and hypotension may be brought on by spinal anaesthesia during caesarean birth. Ephedrine administration does not appear to be as effective in reducing the incidence, occurrence, or severity of hypotension as preventive phenylephrine infusion. Furthermore, compared to ephedrine, inj. phenylephrine appears to be associated with a healthier foetal acid-base state.

Brooker RF et al (1997) (48)conducted a prospective, double-blind, randomized study to treat hypotension following hyperbaric tetracaine (10 mg) spinal anaesthesia in 13 patients, epinephrine and phenylephrine infusions were given. They ultimately came to the conclusion that phenylephrine reduces HR and cardiac output but restores the systolic blood pressure, mean blood pressure, and diastolic blood pressure when used to treat tetracaine spinal-induced hypotension.

Bhattarai B et al (2010)(49) compared the three vasopressors in 90 females undergoing elective caesarean section. P group received 25mcg inj. phenylephrine i.v., E group received 5mg inj. ephedrine and M group received 6mg inj. mephentermine i.v. post spinal hypotension. After the bolus, the heart rate in the phenylephrine group significantly decreased, but there was tachycardia after the bolus administration of ephedrine and mephentermine. It was discovered that the rise in blood pressure was significantly higher in the case of the phenylephrine group in the first six minutes. All three groups' neonatal APGAR scores were comparable.

MATERIALS AND METHODS

Study Design: Randomized, Double-Blind Study.

Organisation of study: Santosh Deemed to be University

Place of study: Department of Anaesthesiology, Santosh Hospital, Ghaziabad

Duration of study: 1 year

Sample Size: 42

n= 21 in each group.

Group I- Patients receiving IV bolus of phenylephrine 100 mcg

Group II- Patient receiving IV bolus of mephentermine 6 mg

Inclusion criteria:

1. All parturients of ASA I & II

Exclusion criteria :

1. Patients suffering from pregnancy induced hypertension.

METHODOLOGY

After obtaining approval by the Institutional Ethical Committee 42 ASA 1 or 2 parturient women admitted to Santosh Medical College scheduled to undergo elective caesarean section under spinal anaesthesia, will be randomly divided into 2 groups of 21 each, fulfilling the criteria of hypotension during the operation as defined. Randomisation was done using a computer generated randomisation chart .

- **Group I**- Patients receiving IV bolus of phenylephrine 100 mcg
- **Group II**- Patient receiving IV bolus of mephentermine 6 mg

Hypotension after spinal anaesthesia is defined as a fall of >20% from baseline or an absolute value of < 100 mmHg of systolic blood pressure, whichever is higher.

METHOD

Preanesthetic Check-up:

The study participants were explained in detail about the study in the language and manner they could understand and Voluntary written informed consent was obtained from each one of them. Pre-anaesthetic assessment was done a day prior to the study. All patients were kept nil per oral for at least 6 hours, premedicated with oral ranitidine 150 mg, and metoclopramide 10 mg were given the night before surgery.

Procedure

Drugs under study for treatment of anticipated hypotension during caesarean delivery were prepared, inj. mephentermine was prepared by adding distilled water solution to make each dose of equal volume and the concentration of 6 mg/ml and phenylephrine 100 mcg/ml was taken. This will be done by an anaesthesiologist who is blind to the study. Identical unlabelled syringes loaded with the drugs were put in labelled tray. As an intervention to treat hypotension as per the study design, each participant was allocated to receive either bolus IV injection of phenylephrine 100 mcg or mephentermine 6 mg. The allocation was done by opaque sealed envelope technique. The registration number of each participant was kept by the anaesthesiologist blind to the study. The investigator was unaware of the specific vasopressor each participant was receiving till the conclusion of the whole trial and collection of data from all the participants

On arrival of the patients in operation theatre, IV line was secured with 18-G cannula; all patients receive 20 ml/kg of Ringer's lactate solution intravascular loading before spinal anaesthesia**,** thereafter this was continued at a rate of approximately 10-15 ml/min throughout the study period. A previously calibrated multi- parameter monitors with Pulse oximeter probe, ECG electrodes, Automated occilometric pressure cuff and temperature probe was attached. Heart rate (HR), non-invasive blood pressure(NIBP), respiratory rate(RR), ECG and peripheral oxygen saturation (SpO_2) were monitored for the duration of study. Baseline systolic and diastolic blood pressure along with heart rate was also noted. Patient was kept in supine position and with a 15-degree wedge under right hip to reduce supine aortocaval compression,

three readings of blood pressure and heart rate were obtained at three minutes interval. To minimize the influence of anxiety in patients with high initial values, the lowest readings of blood pressure and highest readings of heart rate were taken as baseline values. Urinary catheterization was done with Foleys catheter using standard aseptic technique. The resuscitation and general anaesthesia equipment were checked and kept ready to handle any emergency patient crash situation and as a back-up need for conversion from spinal anaesthesia to general anaesthesia if need be. Drugs and spinal needles of same pharmaceutical brand were used for all the participants with an aim towards standardization. Spinal anaesthesia was administered using the midline approach and maintaining standard aseptic precautions using a 25 Gauge Quincke spinal needle. Bupivacaine 12.5 mg (2.5 mL of 0.5% bupivacaine with dextrose 8% solution was used at a rate of approximately 0.2 mL/sec for spinal anaesthesia. Patient was placed in a supine position with a 15º wedge given under right hip. The following parameters were monitored during the study period: Systolic and diastolic blood pressure every 2 minutes after administration of spinal anaesthesia for next 20 minutes; thereafter every 15 minutes till the completion of caesarean section or at least 45 minutes and subsequently every 30 minutes for rest of the study period. Heart rate and any cardiac rhythm disorder using lead II of electrocardiography. Nausea, vomiting and other undesirable maternal effects. The time to first repeat dose of the drug and number of doses. The time from intrathecal administration of bupivacaine to development of hypotension, from spinal anaesthesia to cord clamping and the duration of surgery Hypotension during the study period is treated with repeated one unit (one ml) solution of the drug which is unknown to the interventionist. Maximum number of doses for both drugs will be limited to 20 considering the product insert guidelines of phenylephrine. In case of severe refractory hypotension thereafter, the participant will be excluded from the study and managed on intention to-treat-basis as per institutional protocol after decoding the code. The usual steps of Caesarean section will be followed. Inj. oxytocin 20U in 5% dextrose will be administered after cord clamping. During the study, shivering was treated with IV tramadol 0.5mg/ kg BW and nausea, vomiting with IV ondansetron 4mg per episode. Bolus IV injection of atropine 0.3 mg was administered as a treatment for inappropriate or serve bradycardia. Hypertension was treated as per institutional protocol. The participant, nurses involved in patient care, the group of anaesthesiologists involved preoperatively or in administering the spinal anaesthesia and monitoring and treating

the patient during the study period along with the other treating team members were unaware of the allocation of the participant and the drug being administered.

The following observation have been made:

- Systolic and diastolic blood pressure every 2 minutes after administration of spinal anaesthesia for next 20 minutes; thereafter every 5 minutes till the completion of caesarean section or at least 45 minutes and subsequently every 30 minutes for rest of the study period.
- Heart rate and any cardiac rhythm disorder using lead II of electrocardiography.
- Nausea, vomiting and other undesirable maternal effects.
- The time to first repeat dose of the drug and number of doses.
- The time from intrathecal administration of bupivacaine to development of hypotension, from spinal anaesthesia to cord clamping and the duration of surgery.
- Apgar score of the neonate was recorded at 1 and 5 minutes.

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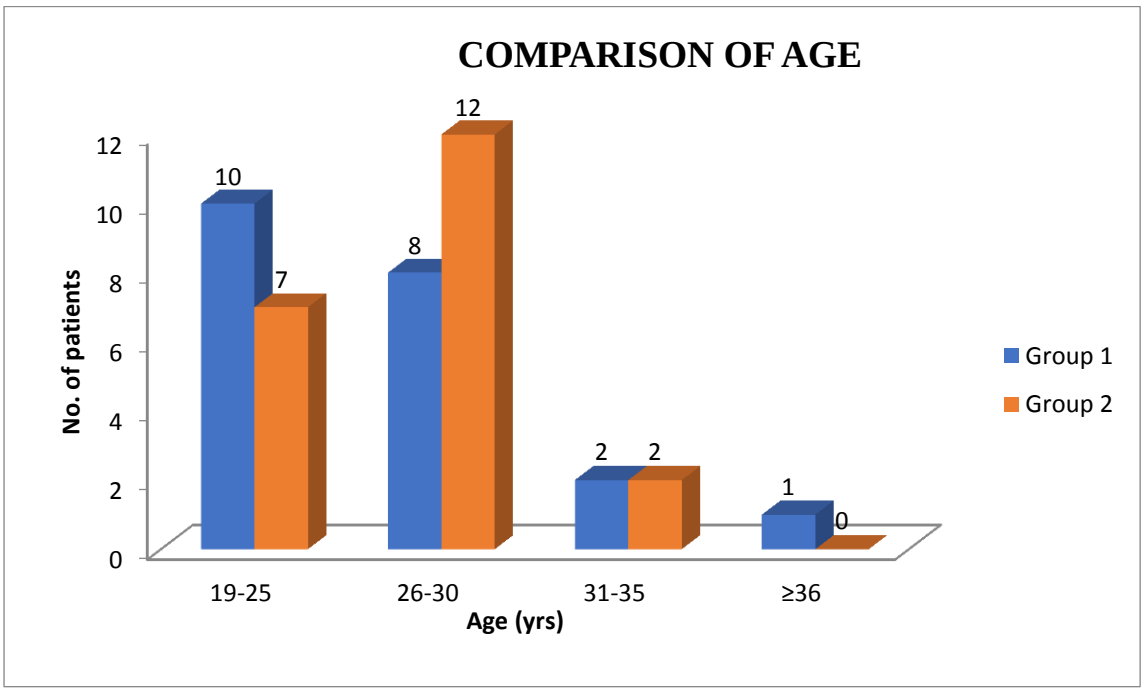
OBSERVATION AND RESULT

TABLE NO. 1 COMPARISON OF AGE

Age (yrs)	Group 1		Group 2	
	N	%	N	%
19-25	10	47.62	7	33.33
26-30	8	38.10	12	57.14
31-35	2	9.52	2	9.52
≥36	1	4.76	0	0.00
Median	27		27	
Range	21-44		19-33	
Mean±SD	27.4±5.0		26.8±3.5	
t & p value	0.457, 0.649 (NS)			

The women in both groups were between 19-44 years of age, and were classified into four subgroups, namely, 19-25 years old, 26-30 years old, 31-35 years old and more than 35 years of age. Majority of patients of Group 1 belonged to 19-25 years age group while for Group 2 the majority of patients belonged to 26-30 years age group. The difference in mean age between the two groups was statistically not significant (p=0.649). (Table no. 1, Graph 1)

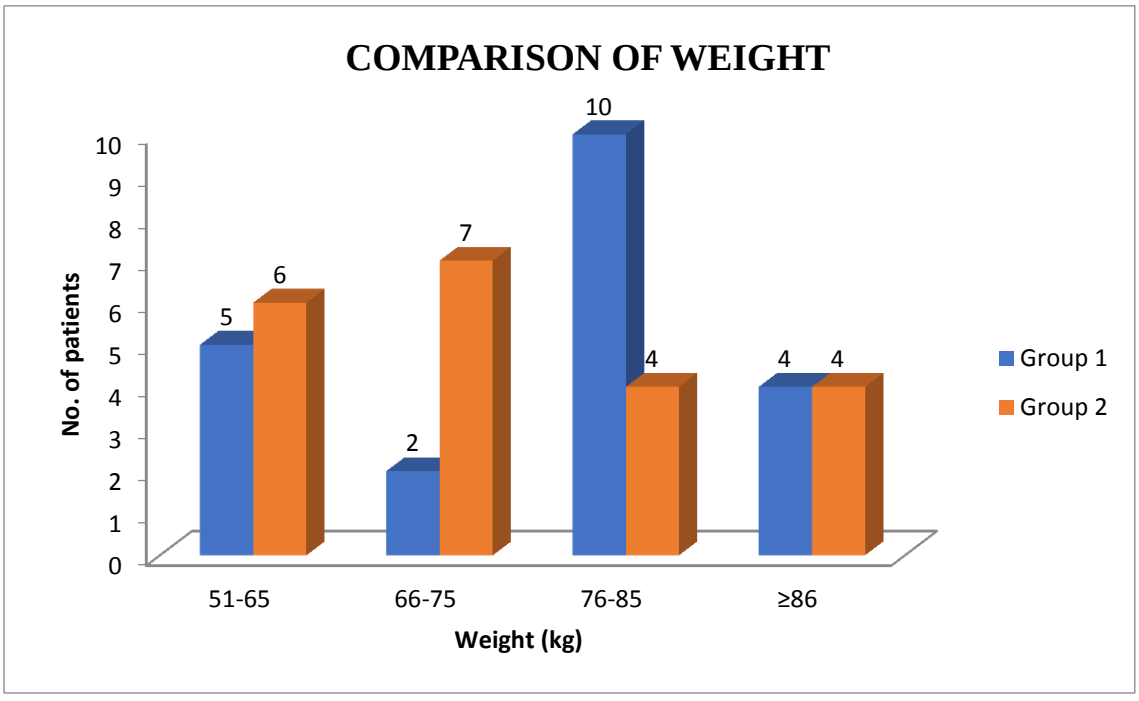


GRAPH 1: COMPARISON OF AGE

TABLE NO. 2 COMPARISON OF WEIGHT

Weight (kg)	Group 1		Group 2	
	N	%	N	%
51-65	5	23.81	6	28.57
66-75	2	9.52	7	33.33
76-85	10	47.62	4	19.05
≥86	4	19.05	4	19.05
Median	78		76	
Range	55-92		51-89	
Mean±SD	76.1±10.6		73.7±12.0	
t & p value	0.679, 0.500 (NS)			

The weight of the subjects in the study ranged from 51 to 92 kgs. Maximum subjects were from the age group of 76-85 kgs. In intergroup comparison, the mean weight of Group 1 was 76.1±10.6 whereas the mean weight of Group 2 was 73.7±12.0. No significant difference was found between Group 1 and Group 2 with respect to weight (p=0.500). (Table no. 2, Graph 2)

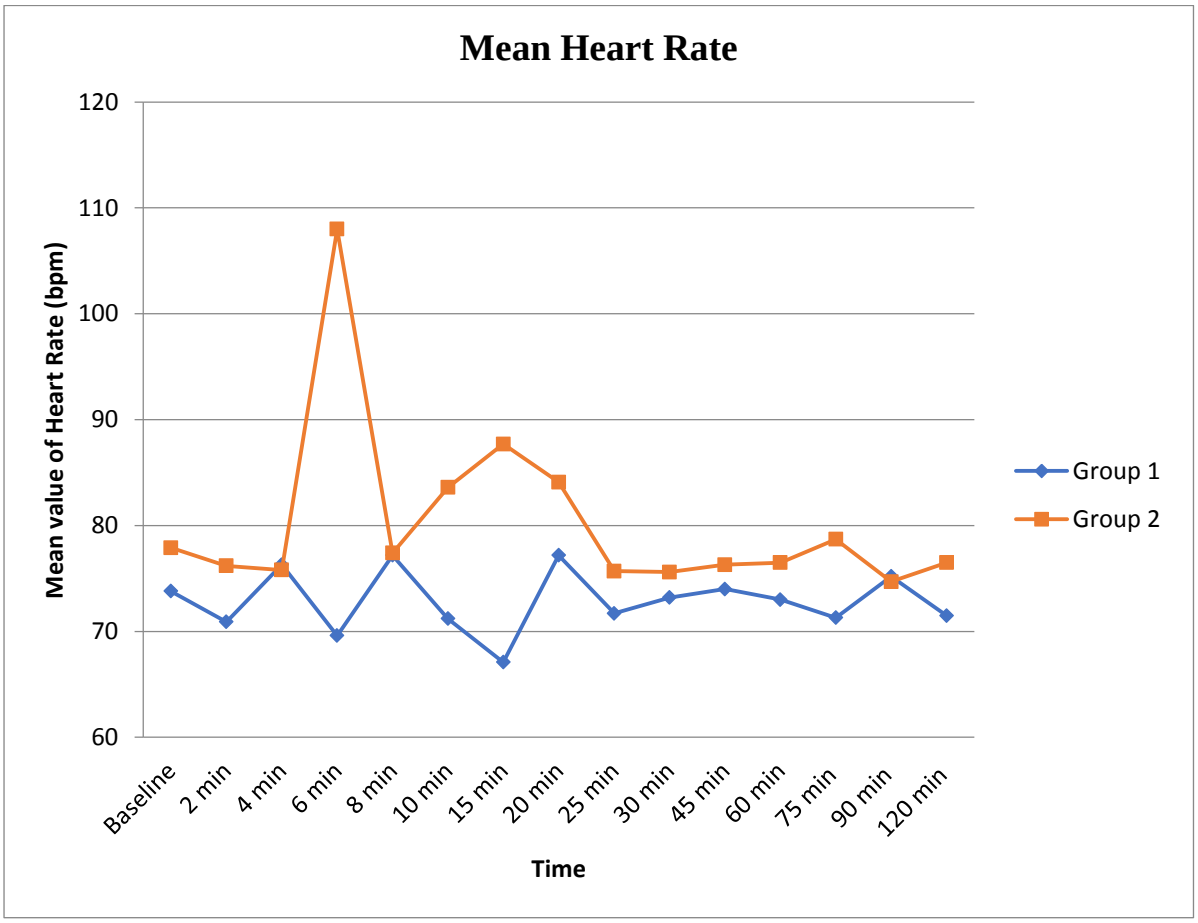


GRAPH 2: COMPARISON OF WEIGHT

TABLE NO. 3 MEAN HEART RATE

Time	HEART RATE (BPM)		t value	p value
	Group 1 (Mean±SD)	Group 2 (Mean±SD)		
Baseline	73.86±10.34	77.9±10.2	1.277	0.208
2 min	70.95±12.36	76.29±11.08	1.472	0.148
4 min	76.38±10.64	75.81±12.37	0.160	0.873
6 min	69.62±13.76	108.71±16.9	8.221	<0.0001
8 min	77.29±10.37	77.42±13.40	0.038	0.969
10 min	71.24±12.39	83.66±14.08	3.036	0.004
15 min	67.14±13.42	87.76±15.6	4.590	<0.0001
20 min	77.29±10.37	84.19±18.31	1.504	0.140
25 min	71.71±12.09	75.76±13.15	1.038	0.305
30 min	73.24±10.65	75.62±10.11	0.743	0.461
45 min	74.05±10.03	76.38±8.85	0.799	0.428
60 min	73.00±9.13	76.57±10.53	1.174	0.247
75 min	71.39±10.61	78.78±13.06	1.768	0.087
90 min	75.22±9.3	74.75±13.89	0.073	0.943
120 min	71.5±8.06	76.5±19.09	0.488	0.651

At baseline, the mean heart rate in Group 1 and Group 2 was 73.86±10.34 BPM and 77.9±10.2 BPM respectively. On comparison at baseline no statistically significant difference was found between both the groups (p=0.208). The mean heart rate in both the groups measured at various time intervals after administration of the vasopressors was analysed by t-test and it was found that the heart rate was significantly higher in Group 2 in comparison to Group 1 at 6^{th} minute (p=<0.0001), 10^{th} minute (p=0.004) and at 15^{th} minute (p=<0.0001). (Table 3, Graph 3)

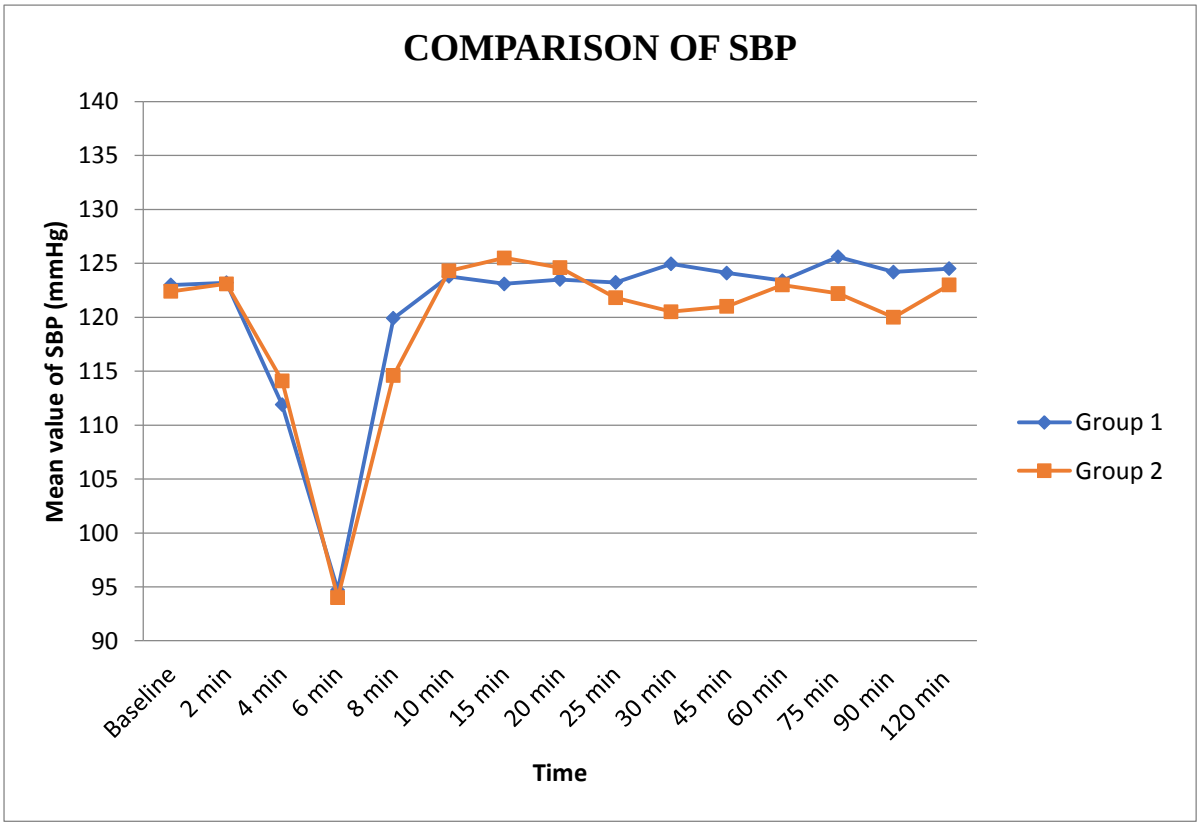


GRAPH. 3 MEAN HEART RATE

TABLE NO. 4 SYSTOLIC BLOOD PRESSURE

Time	SBP (mmHg)		t value	p value
	Group 1 (Mean±SD)	Group 2 (Mean±SD)		
Baseline	123±8.74	122.48±9.61	0.184	0.854
2 min	123.24±9.93	123.14±10.31	0.03	0.975
4 min	111.9±18.15	114.1±15.61	0.419	0.677
6 min	94.71±11.43	94±8.53	0.229	0.819
8 min	119.9±16.03	114.67±13.82	1.134	0.263
10 min	123.81±5.51	124.38±6.89	0.296	0.768
15 min	123.14±6.34	125.52±7.18	1.139	0.261
20 min	123.52±4.69	124.67±7.47	0.594	0.555
25 min	123.23±5.19	121.81±6.78	0.766	0.447
30 min	124.95±7.71	120.52±8.64	1.752	0.087
45 min	124.14±6.78	121.05±6.68	1.490	0.144
60 min	123.43±8.08	123.05±7.74	0.156	0.876
75 min	125.67±6.94	122.29±7.64	1.309	0.200
90 min	124.22±5.61	120±12.33	0.876	0.399
120 min	124.5±2.52	123±1.41	0.755	0.491

The mean SBP in Group 1 at baseline was 123±8.74 mmHg and in Group 2 it was 122.48±9.61 mmHg. After administration of vasopressors, no statistically significant difference was found between both the groups using t test at all the time intervals SBP was measured. (Table 4, Graph 4)

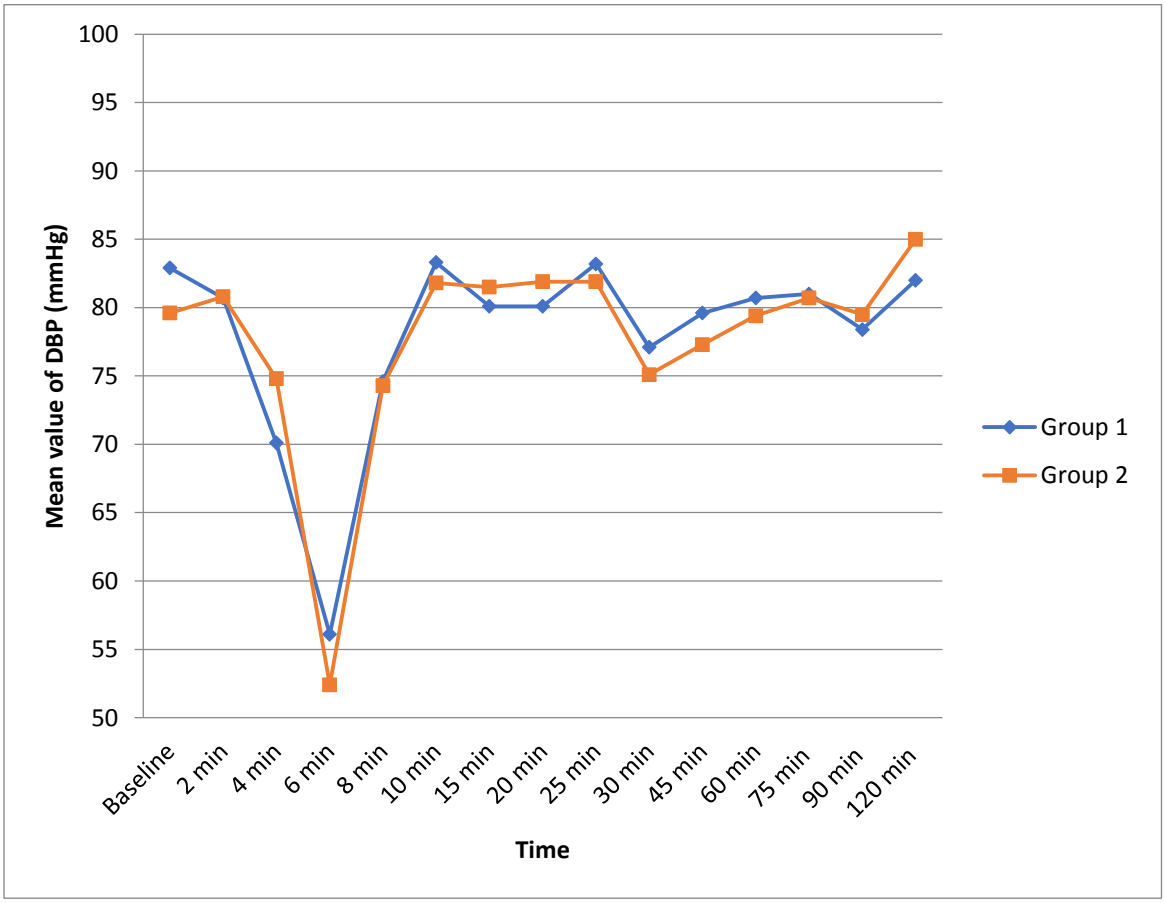


GRAPH 4: COMPARISON OF SYSTOLIC BLOOD PRESSURE

TABLE NO. 5 MEAN DISTRIBUTION OF CASES BY GROUPS AND DIASTOLIC BLOOD PRESSURE

Time	DBP (mmHg)		t value	p value
	Group 1 (Mean±SD)	Group 2 (Mean±SD)		
Baseline	82.95±4.32	79.62±7.81	1.711	0.094
2 min	80.76±7.2	80.86±7.09	0.043	0.965
4 min	70.19±15.46	74.86±14.6	1.006	0.320
6 min	56.19±12.96	52.48±7.01	1.155	0.254
8 min	74.67±15.95	74.38±16.07	0.057	0.954
10 min	83.33±5.03	81.81±6.06	0.886	0.380
15 min	80.1±5.46	81.52±5.65	0.833	0.409
20 min	80.19±5.17	81.9±6.08	0.983	0.331
25 min	83.24±3.92	81.9±5.35	0.921	0.362
30 min	77.14±6.74	75.14±5.08	1.086	0.284
45 min	79.62±5.71	77.33±5.42	1.33	0.190
60 min	80.76±5.04	79.43±6.76	0.724	0.472
75 min	81.00±6.48	80.71±6.45	0.124	0.902
90 min	78.44±7.33	79.5±10.38	0.213	0.350
120 min	82.00±1.63	85.00±1.41	2.191	0.093

The mean value of diastolic BP at baseline was greater Group I (82.95±4.32 mmHg) than Group II (79.62±7.81), but the difference was not significant (p=0.09. All time points following the delivery of vasopressors saw statistically negligible differences in the two groups' mean values of diastolic blood pressure. (Table 5, Graph 5).

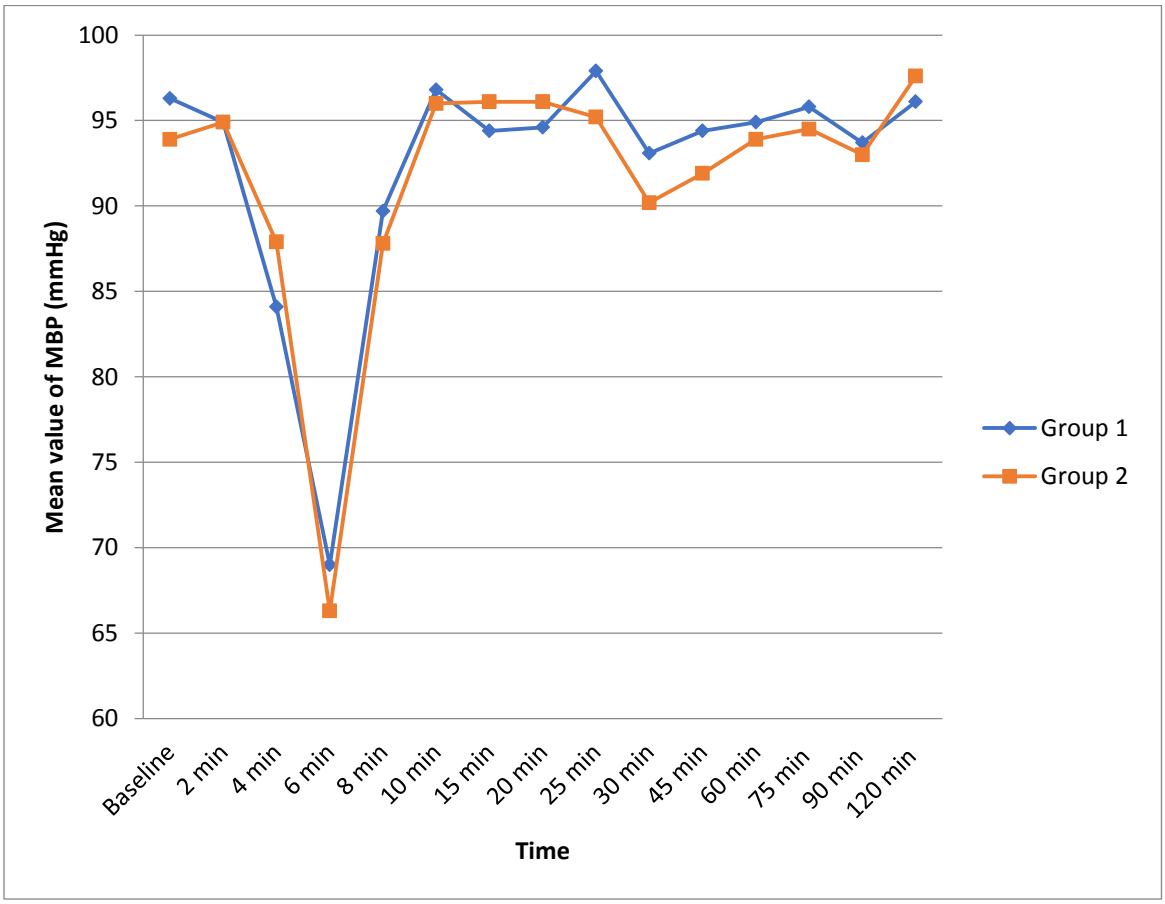


GRAPH 5: COMPARISON OF DIASTOLIC BLOOD PRESSURE

TABLE NO. 6 COMPARISON OF MEAN BLOOD PRESSURE

Time	MBP (mmHg)		t value	p value
	Group 1 (Mean±SD)	Group 2 (Mean±SD)		
Baseline	96.3±5.11	93.9±7.22	1.225	0.227
2 min	94.92±7.14	94.95±7.9	0.0205	0.983
4 min	84.1±15.78	87.94±14.57	0.831	0.410
6 min	69.03±11.55	66.32±6.88	0.911	0.367
8 min	89.75±15.77	87.81±15.1	0.389	0.699
10 min	96.83±4.93	96±5.14	0.492	0.624
15 min	94.44±5.13	96.19±5.51	1.102	0.277
20 min	94.63±4.36	96.16±5.72	0.99	0.327
25 min	97.9±3.63	95.21±5.63	1.893	0.656
30 min	93.08±6.07	90.19±5.35	1.644	0.108
45 min	94.46±5	91.9±5.05	1.687	0.099
60 min	94.97±5.16	93.97±6.28	0.614	0.542
75 min	95.89±6.11	94.57±6.44	0.614	0.543
90 min	93.7±5.64	93±10.59	0.15	0.883
120 min	96.17±1.14	97.67±1.41	1.854	0.137

The mean value of MBP was compared in both the groups, from baseline till the end of the surgery, at baseline the p value was 0.277 and during the intraoperative period the p value was greater than 0.05, thus there was no statistical difference between both the groups. (Table 6, Graph 6)



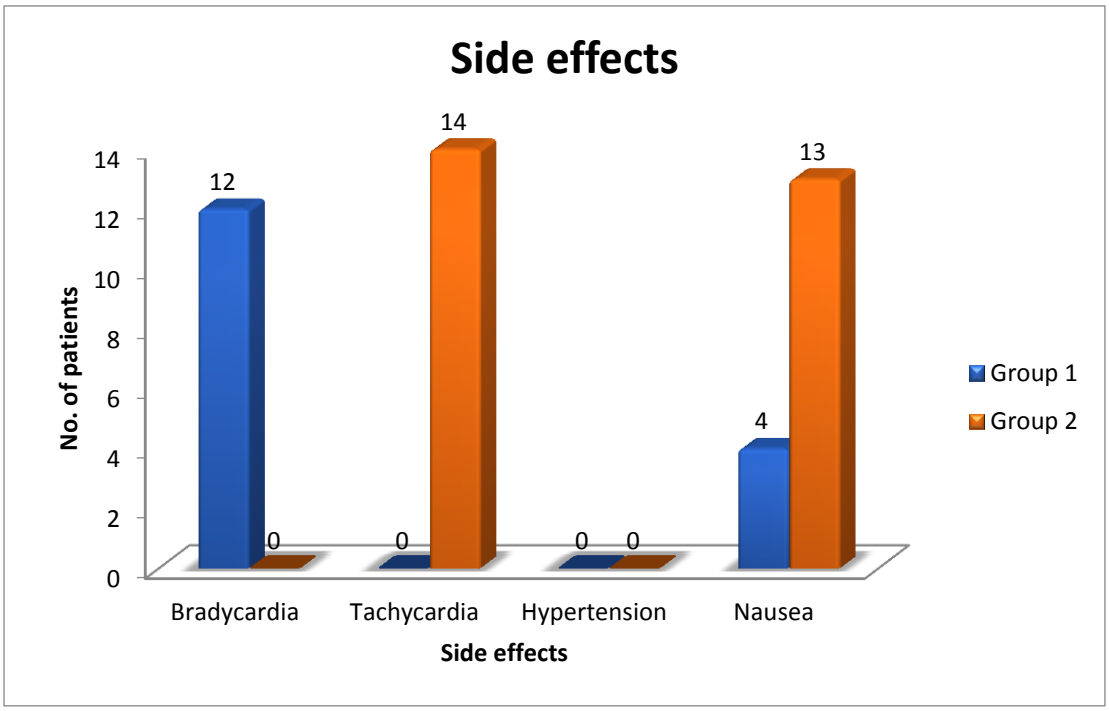
GRAPH 6: COMPARISON OF MEAN BLOOD PRESSURE

TABLE NO. 7 COMPARISON OF INCIDENCE OF SIDE EFFECTS BETWEEN GROUPS

Side effects	Group 1		Group 2		P value
	N	%	N	%	
Bradycardia	12	57.14	0	0.00	<0.0001
Tachycardia	0	0.00	14	66.67	<0.0001
Hypertension	0	0.00	0	0.00	-
Nausea	4	19.05	13	61.90	0.004

Chi square test & Fisher exact test

In Group 1, bradycardia and nausea was developed by 57.14% and 19.05% of patients respectively while no patient developed tachycardia or hypertension. In Group 2, side effects viz. tachycardia and nausea occurred in 66.67% and 61.90% patients respectively whereas bradycardia and hypertension did not develop in any patient. On comparing both the groups, the difference between both the groups in the development of bradycardia (p<0.0001), tachycardia (p<0.0001) as well as nausea (p=0.004) was statistically significant. (Table 7, Graph 7)



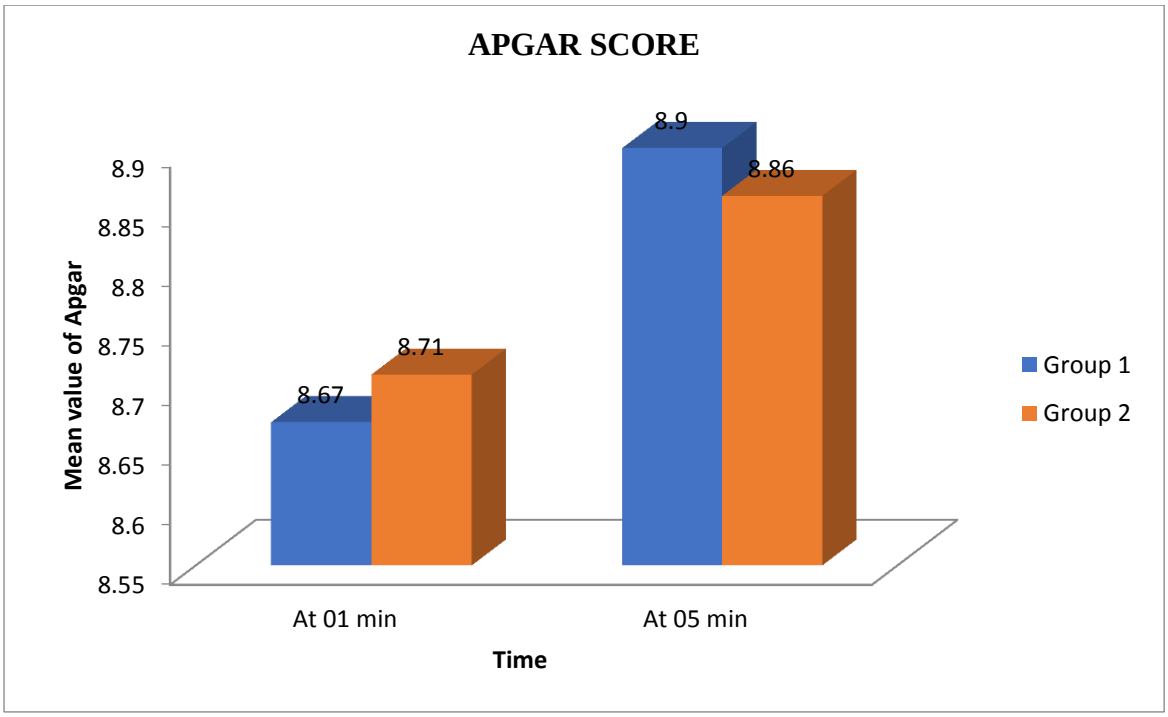
GRAPH 7: COMPARISON OF INCIDENCE OF SIDE EFFECTS BETWEEN GROUPS

TABLE NO. 8 APGAR SCORE

Time	APGAR score		t value	p value
	Group 1 (Mean±SD)	Group 2 (Mean±SD)		
At 01 min	8.67±0.48	8.71±0.46	0.326	0.746
At 05 min	8.9±0.3	8.86±0.36	0.466	0.643

At 1 minute, the mean APGAR score in Group 1 was 8.67±0.48, whereas in Group 2 was 8.71±0.46. At 5 minutes, it increased to 8.9±0.3 in Group 1 and to 8.86±0.36 in Group 2.

On comparing both the group's Apgar scores using t test no statistically significant difference was found in both the groups at 1 minute (p=0.746) as well as 5 minutes (p=0.643). (Table 8. Graph 8)



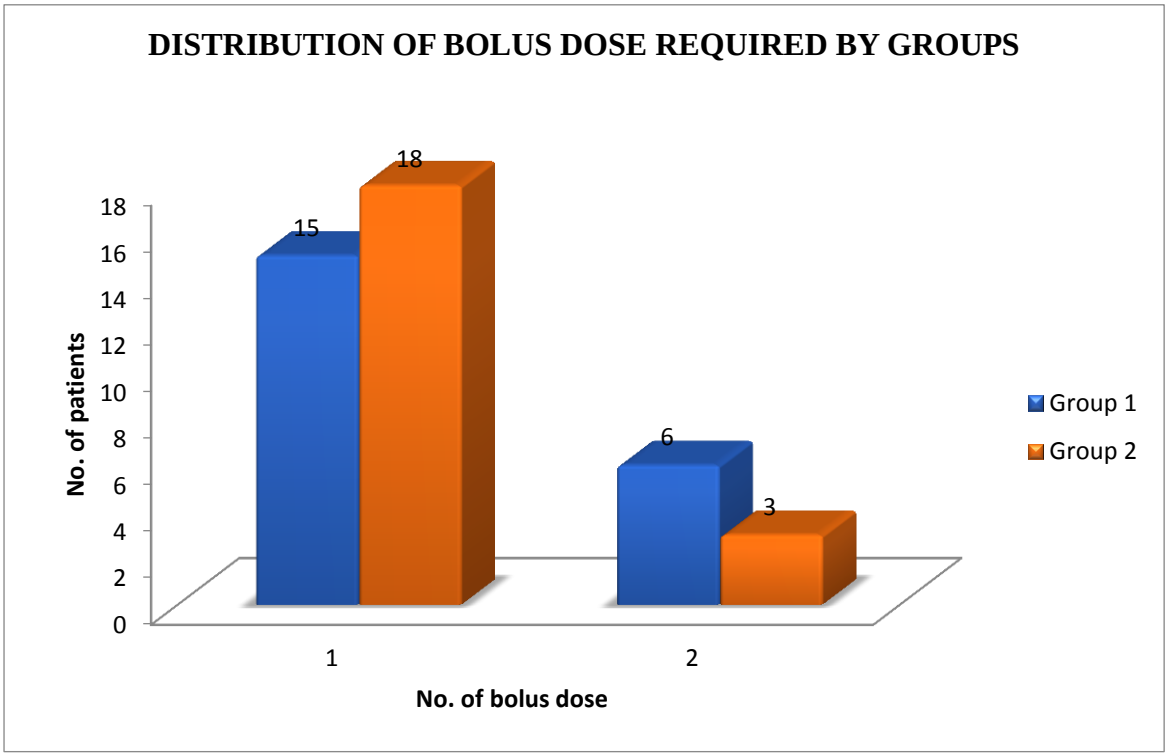
GRAPH 8: APGAR SCORE

TABLE NO. 9 DISTRIBUTION OF BOLUS DOSE REQUIRED BY GROUPS

No. of Bolus dose	Group 1		Group 2	
	N	%	N	%
1	15	71.43	18	85.71
2	6	28.57	3	14.29
Total	21	100.00	21	100.00

Fisher exact test, P value 0.453 (NS)

In group 1 - 71.43% of the parturients needed 1 bolus dose and the remaining 28.57% of the parturients needed 2 bolus doses to maintain systolic pressure. In group 2 - 85.71% of the parturients needed 1 bolus dose and 14.29% of the parturients needed 2 bolus doses to maintain systolic pressure blood pressure. There was no statistical difference between the two groups (p=0.453) in terms of required bolus dose. (Table 9, Graph 9)



GRAPH 9: DISTRIBUTION OF BOLUS DOSE REQUIRED BY GROUPS

STATISTICAL ANALYSIS

The data collected during the study was compiled using a Microsoft Excel spread sheet and analyzed statistically using the statistical package for the MedCalc statistical Software version 20.115 for window editions. Qualitative data were presented as number, percentage and Quantitative data were presented as mean±SD and median. Comparison between groups was done by $\chi 2$-test, fisher exact test and unpaired t test. P value less than 0.05 was considered to be statistically significant.

DISCUSSION

The present study "A Comparative study of mephentermine and phenylephrine in the treatment of hypotension during spinal anaesthesia for caesarean section" was carried out at Santosh Medical College and Hospital between 2020-2023.

The aim of the study was to evaluate and compare the effectiveness of phenylephrine and mephentermine in the treatment of spinal induced hypotension in the caesarean section surgery, and also to observe and compare the side effects of the two vasopressor agents. The effect of these drugs on neonatal APGAR score is also noted.

This study was carried out on 42 pregnant female undergoing elective caesarean section under spinal anaesthesia, after approval of the Institutional Research Committee. The patients were randomly divided in to two groups. The subjects who developed post spinal hypotension in a caesarean section were divided into two groups. Group I, patients received 100 mcg Phenylephrine intravenously. In Group II, patients received Inj. Mephentermine 6mg intravenously. After administration of drugs various parameters were studied and observed.

Both groups' baseline characteristics and demographic information were equivalent. Between the groups, the hemodynamic indicators at the onset of hypotension were also similar. The age of the females ranged from 19-44 years, it was further classified into four sub groups 19-25, 26-30, 31-25 and 36 and above. The median of group I and group II was 27. The mean of group I 27.4±5.0 and group II 26.8±3.5. On using t test an insignificance difference was found (p value=0.649).

The weight of the females int the study ranged from 51 to 92 kgs. The median of group I was 78 and group II was 76. On comparing the mean weight the values were found out to be 76.1±10.6 for group I and 73.1±12.0 for group II. There was no statistical difference between both the group(p=0.500).

SBP, DBP and MAP

The systolic blood pressure was monitored throughout the surgery from baseline till the end of the surgery. The baseline value of SBP was comparable between two groups with the difference in mean values being statistically insignificant (p=0.856).

After administration of Phenylephrine in group I and Mephentermine in group II, there was no statistical difference at any point of time during the surgery. The p value was greater than 0.05. The mean value of DPB (diastolic blood pressure) at the baseline was compared in both the groups and if was observed that mean was greater in Group I (82.95±4.32 mmHg) than Group II (79.62±7.81), but the difference was not significant (p=0.09). During intra-operative period the diastolic blood pressure was comparable in both the groups. From the beginning of the surgery to the end of it, the mean value of MAP in both groups was comparable. Hence, it shows that both the vasopressors have similar effect on the systolic, diastolic and mean blood pressure of the females developing hypotension post spinal in a caesarean section.

Kansal A et al (17) studied the efficacy of Mephentermine and Ephedrine in maintaining arterial pressure in females who underwent caesarean section surgery and received subarachnoid block. They concluded that after administration of both the drugs there was no statistically significant difference between them in terms of induced haemodynamic changes.

Smith N et al(50) administered Mephentermine in 5 patients to study the changes in haemodynamics by it and concluded that a single dose of Mephentermine increases MAP, vascular resistance as well as cardiac work without causing a change in other parameters like heart rate implying that Mephenrermine produces increase in arterial pressure while causing only minimal changes in heart rate.

Warwick D et al(51) reviewed various studies to on prevention and management of hypotension and found that recent literature suggests using phenylepherine α-agonists in management of hypotension. Alahutta S et al(52) compared Ephedrine and Phenylephrine as a treatment for maintaining the systolic arterial pressure twenty percent more than the baseline in patients undergoing LSCS surgery performed under subarachnoid block. They concluded that both the drugs were equally effective in increasing arterial pressures more than twenty percent above baseline.

Heart Rate

The heart rate (HR) of subjects was monitored throughout the surgery from baseline to 120^{th} min in both the groups. The mean value at baseline of Group I and Group II was 73.86±10.34 BPM and 77.9±10.2 BPM respectively. At baseline there was no

statistical difference (p=0.208), but at the 6^{th} 10^{th} and 15^{th} min, after the administration of vasopressors it was found out that the heart rate was higher in the group II. At 6^{th} minute p value was <0.0001, at 10^{th} minute p value was 0.004 and at 15^{th} minute p value was <0.0001 which shows statistical significance.

Bradycardia, Tachycardia, Hypertension

In our study twelve patients developed bradycardia after administration of Phenylephrine (Group I) whereas no patient developed it after administration of Mephentermine (Group II). Fourteen patients in Group II developed tachycardia while no patient developed tachycardia in Group I. In Group I no patient hypertension. In addition to this, in Group II no patients experienced hypertension as well. When comparing the two groups, there was a statistically significant difference in the development of bradycardia (p=0.0001), tachycardia (p=0.0001). Therefore, in patients there is more bradycardia when phenylephrine is used, while mephentermine causes tachycardia. This effect can be attributed to Mephentermine's direct as well as indirect action in contrast to Phenylephrine which acts directly on the α receptors.

Several studies have also reported then same changes as we observed in our study. In a study carried out by Dinesh Sahu et al(36) it was observed that the bolus dose of phenylephrine causes a decrease in the heart rate.

Nausea

Nausea was present in both the groups but higher incidence in the mephentermine group. In our study 19.05% of patients who received Phenylephrine developed nausea whereas 61.90% of patients who received Mephentermine developed nausea. When both groups were compared, patients in Group II had statistically significant incidence of nausea as compared to Group I (p=0.004).

Dinesh Sahu et al(36) in their study found observed that 10% subjects who were administered Phenylephrine experienced nausea and 15% of subjects in Mephentermine group experienced nausea which is in contrast to our study. Moran DH et al (37) observed in their study that the difference in nausea and vomiting in patients who were administered either Ephedrine or Phenylephrine was statistically insignificant. In a study conducted by Turkoz A et al (53) six percent of patients

receiving Ephedrine infusion developed nausea while sixty-six percent of patients receiving Ephedrine bolus developed nausea.

Bolus Dose

In our current study, 71.43% of patients in group I required a single bolus dose of the vasopressor and 85.71% of patients in group II required a single bolus dose to maintain systolic blood pressure above 20% of basal value. Rest patients in both the groups required 2 bolus doses to achieve the desirable effect. Regarding the necessary bolus dosage, there was no statistical difference between the two groups (p=0.453).

APGAR

The APGAR score at 1^{st} min and 5^{th} min was above 8, therefore both the drugs have no neonatal adverse effects. At one minute, Group I's mean APGAR score was 8.67±0.48 while Group II's was 8.71±0.46. It increased to 8.9±0.3 in Group I and 8.86±0.36 in Group II at 5 minutes. When comparing the APGAR scores of the two groups using a t test, there was no statistically significant difference between the groups at 1 minute or at 5 minutes (p=0.746).

Dinesh Sahu et al(36) on comparing the APGAR scores found that both Phenylephrine and Mephentermine treatment groups had APGAR score of more than 7 of neonates.

SUMMARY

This comparative, randomized control study was conducted to assess the efficacy of Mephentermine versus Phenylephrine for treating hypotension during caesarean section surgery under subarachnoid block. Spinal anaesthesia induced hypotension may prove deleterious to both mother and baby, hence vasopressors play a vital role in their management. Parameters such as on SBP, DBP and MAP were measured, furthermore, the incidence of undesirable side effects i.e., bradycardia, tachycardia, hypertension, and nausea were also evaluated. Neonatal outcome in terms of Apgar score was also studied.

In our study all the subjects had similar demographics, our study population was parturient females undergoing elective caesarean section and their age group ranged from 19-44 years. There was unbiased division of females on the basis of their weight with their weight ranging from 51 to 92 kgs. The result of our study suggested that phenylephrine and mephentermine are equally potent drugs, both the drugs maintained the blood pressure within 20% of baseline values. The effect on mean SBP, mean DBP, and MAP was comparable in both the groups at different time intervals with a p value of <0.05 suggesting a statistically insignificant difference. The heart rate of all the subjects were comparable in both the groups at the baseline (p=0.208) with a mean value of 73.86±10.34 BPM in Group I and 77.9±10.2 BPM in Group II. In our study we also noticed the subjects who received bolus of phenylephrine developed brachycardia which did not go below 50/min, it was not treated by IV atropine, and the lower heart rate was proved beneficial to counter the undesirable tachycardia, while mephentermine bolus lead to tachycardia. During the intraoperative time after the administration of bolus dose of respective vasopressors it was noted that the phenylephrine group had more number of subjects (n=12, 57.14%) who suffered bradycardia while no subject developed bradycardia in Group 2. In the mephentermine group it was observed that there were more number of patients (n=14, 66.67%) who suffered tachycardia, whereas no patient developed tachycardia in Group I. None of the groups had an episode of reactive hypertension. Both the groups had episodes of nausea i.e., 19.05% of patients in Group I and 61.90% of patients in Group II. On statistical analysis Group 2 had significantly higher incidence of nausea (p=0.004). The number of boluses required in both the groups were also similar, while

mephentermine required less second bolus, but there was no statistical difference (p=0.453). The neonatal APGAR in both the groups remained above 8 at 1st and 5th minute, which signified that both the drugs have no impact on the neonatal outcome (At 1st minute p=0.746, at 5th minute p=0.643). In our study the potency of both the drugs was observed equal in treating the post spinal hypotension in females undergoing caesarean section at all the time intervals.

CONCLUSION

This comparative study demonstrated that both the vasopressors namely Mephentermine and Phenylephrine through intravenous route have similar efficacy in maintenance of post spinal maternal hypotension during a caesarean section, although Phenylephrine causes reduction in heart rate which can be of advantage in patients with undesirable tachycardia, in comparison to Mephentermine. Both the vasopressor had no significant adverse effects and the APGAR score remained above 8 in both the groups.

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ANNEXURE 1

PROFORMA

1. GENERAL INFORMATION

Name	
Age (in years)/ Sex	
Occupation	
Address	
Diagnosis	
Operation proposed	
MRD No.	
Surgery Unit	
Date	

2. GENERAL EXAMINATION

General Condition	
Any positive history	
Heart Rate(beats per minute)	
Blood Pressure (in mm of Hg)	
Temperature (in degree Fahrenheit)	
Spo2 (in %)	
Mouth Opening	
MPG grade	
Neck movement	
Oral examination	
ASA Grade	

3. SYSTEMIC EXAMINATION:

System	Findings
Respiratory system	
Cardiovascular system	
Central nervous system	
Per abdomen(G.I system)	

4. ANY SYSTEMIC DISEASE:

5. INVESTIGATIONS:

6. DEMOGRAPHIC PARAMETERS:

Parameters	
Age	
Weight (BMI)	
Height	
Duration of surgery	

7. GROUP ALLOCATON:

GROUP I:	
GROUP II:	

8. PERIOPERATIVE HEMODYNAMIC CHANGES

TIME	BP					
	SBP		DBP		MAP	
	I	II	I	II	II	I
BASELINE						
AFTER SPINAL						
2 min						
4 mins						
6 mins						
8 mins						
10 mins						
15 mins						
20 mins						
25 mins						
Upto 120 min						

9.SIDE EFFECT PROFILE OF DRUGS

SIDE EFFECT	GROUP I	GROUP II
HYPOTENSION		
TACHYCARDIA		
BRADYCARDIA		
NAUSEA		

10. APGAR SCORE AT 0 AND 5 MINUTES

	TIME			
	0 MIN		5 MIN	
	I	II	I	II
APGAR SCORE				

ANNEXURE 2

CONSENT FORM

I, _____ Son/ Daughter/ Wife of _____ Resident of _____ Hereby declare that I give my full, free and voluntary informed consent in the thesis **A Comparative Study of Mephentermine and Phenylephrine in the Treatment of Hypotension During Spinal Anaesthesia for Caesarean Section** Dr._____ has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various laboratory investigations for the study to be carried out. I have been informed about the duration of the study and instructions to be followed during the study period. I give full consent for being enrolled in the above study and I reserve my rights to withdraw from this study, whenever I wish without prejudice of my right to undergo further treatment at Santosh Hospital, Ghaziabad U.P.

Patient's/ Patient's relative's signature Doctors signature

Or thumb impression

Name: Date:

We have witnessed that the patient signed the above form in the presence of his free will after fully understanding its content.

1.	2.
Signature of Witness	Signature of Investigator
Name	Name:

Dr. Jahnavi Tomar
Post graduate Student
Batch 2020 - 2023
Santosh Medical College & Hospital
Ghaziabad – 201001 (U.P.)

ANNEXURE 3

संतोष मेडिकल कॉलेज एवं अस्पताल (गाजियाबाद)

सूचित सहमति

मैं _____ बेटा_____

निवासी_____ घोषणा करता हूं कि मुझे डॉ._____, ने मुझे मेरी भाषा में अपने अध्ययन, अध्ययन के उद्देश्य के बारे मे, और अध्ययन के दौरान अपना ईजाज वाली विभिन्न प्रयोगशाला जांच के बारे में सूचित कर दिया है। मुझे अध्ययन की अवधि और उसके दौरान अपनाए जाने वाले निर्देश भी मेरी भाषा मे समझा दिए गए हैं| मैं उपरोक्त अध्ययन में बिना किसी दबाव के दाखिला ले रहा हूं और पूर्ण सहमति दे रहा हूं| सन्तोष अस्पताल, गाजियाबाद में अपने आगे के उपचार पर बिना प्रतिकूल प्रभाव डाले इस अध्ययन से और प्रयोगशाला जांच की प्रकृति से मैं जब चाहूँ बाहर जाने के अपने अधिकार को सुरक्षित रख रहा हूं

रोगी / रोगी के रिश्तेदार के हस्ताक्षर डॉक्टर के हस्ताक्षर या अंगूठे का निशान

नाम

नांक:

मेरी उपस्थिति में मरीज ने पूरी तरह से डाकटर के बताए गए अध्ययन और निर्देशों को समझने के बाद अपनी स्वतंत्र इच्छा से ऊपरके फार्म पर हस्ताक्षर कि ए हैं।

Signature of Investigator
Dr. Jahnavi Tomar
Post graduate Student
Batch 2020- 2023
Santosh Medical College & Hospital
Ghaziabad – 201001 (U.P)

ANNEXURE 4

LIST OF ABBREVIATIONS

1.	ANS	–	AUTONOMIC NERVOUS SYSTEM
2.	APGAR	–	APPEARANCE, PULSE, GRIMACE, ACTIVITY AND RESPIRATION
3.	ASA	–	AMERICAN SOCIETY OF ANAESTHESIOLOGY
4.	C- SECTION	–	CESEAREAN SECTION
5.	CNS	–	CENTRAL NERVOUS SYSTEM
6.	CSF	–	CERBROSPINAL FLUID
7.	CVS	–	CARDIOVASCULAR SYSTEM
8.	DBP	–	DIASTOLIC BLOOD PRESSURE
9.	DOA	–	DURATION OF ANALGESIA
10.	ECG	–	ELECTROCARDIOGRAM
11.	HR	-	HEART RATE
12.	I M	–	INTRA MUSCULAR
13.	I V	–	INTRA VENOUS
14.	LSCS	–	LOWER SEGMENT CESEREAN SECTION
15.	MAP	–	MEAN ARTERIAL PRESSURE
16.	NIBP	–	NON-INVASIVE BLOOD PRESSURE
17.	SBP	–	SYSTOLIC BLOOD PRESSURE
18.	SC	–	SUBCUTANEOUS
19.	SPO2	–	OXYGEN SATURATION

ANNEXURE 5

ETHICAL COMMITTEE CLEARANCE

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[43] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic **"COMPARISON OF PHENYLEPHRINE HYDROCHLORIDE INFUSION AND MEPHENTERMINE SULPHATE FOR PREVENTION OF POST SPINAL HYPOTENSION IN CESAREAN SECTION."**, submitted by **Dr. Jahnavi Tomar,** MD/MS student of Batch 2020-2021, Department of **Anaesthesia**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"COMPARISON OF PHENYLEPHRINE HYDROCHLORIDE INFUSION AND MEPHENTERMINE SULPHATE FOR PREVENTION OF POST SPINAL HYPOTENSION IN CESAREAN SECTION."**, **Dr. Jahnavi Tomar** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

SANTOSH DEEMED TO BE UNIVERSITY REGISTRAR GHAZIABAD, NCR (U.P.)

Dr. Jahnavi Tomar
MD/MS student of batch 2020-2021
Department of Anaesthesia
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Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr. Subrata Dutta (Guide)
7. HOD of **Anaesthesia**

ANNEXURE 6

PLIAGARISM CERTIFICATE

Ouriginal
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| S. No. | Group | Age (yrs) | Weight (kg) | Baseline | | | | 2 mins | | | | 4 mins | | | | 6 mins | | | | 8 mins | | | | 10 mins | | | | 15 mins | | | | 20 mins | | | | 25mins | | | | 30 mins | | | | 45 mins | | | | 60 mins | | | | 75 mins | | | | 90 mins | | | | 120 mins | | | | Bolus Dose | Brachycardia | Tachycardiya | Hypertension | Nausea | Apgar score | |
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